

21 66/7/1-9

6/7/1 (Item 1 from file: 399)

1101095E2 CA: 1101151129858 JOURNAL

Deletion screening of the Duchenne muscular dystrophy locus via multiplex DNA amplification

AUTHOR(S): Chamberlain, Jeffrey S.; Gibbs, Richard A.; Ranier, Joel E.; Nguyen Thi Nga; Caskey, C. Thomas

LOCATION: Inst. Mol. Genet., Baylor Coll. Med., Houston, TX, 77030, USA

JOURNAL: Nucleic Acids Res. DATE: 1988 VOLUME: 16 NUMBER: 23 PAGES:

11141-5E CODEN: NARHAD ISSN: 0305-1048 LANGUAGE: English

SECTION:

CA203005 Biochemical Genetics

CA213XXX Mammalian Biochemistry

CA214XXX Mammalian Pathological Biochemistry

IDENTIFIERS: Duchenne muscular dystrophy deletion mutation screening, human Duchenne muscular dystrophy diagnosis, DNA multiplex amplification gene deletion screening

DESCRIPTORS:

Deoxyribonucleic acid...

Isogenic multiplex amplification of, in screening for Duchenne muscular dystrophy gene deletions, in human

Gene and genetic element, animal...

For Duchenne muscular dystrophy, of human, rapid screening method for deletions in, multiplex DNA amplification in

Muscular dystrophy, Duchenne...

For, of human, rapid screening method for deletions in, multiplex DNA amplification in

Mutation, deletion...

In Duchenne muscular dystrophy gene, of human, screening method for, multiplex DNA amplification in

Deoxyribonucleic acid sequences...

Of Duchenne muscular dystrophy gene deletion-prone exons and flanking introns, of human

6/7/2 (Item 2 from file: 399)

108162604 CA: 1081191162604a JOURNAL

Expression of the murine Duchenne muscular dystrophy gene in muscle and brain

AUTHOR(S): Chamberlain, Jeffrey S.; Fearlman, Joel A.; Muzny, Donna M.; Gibbs, Richard A.; Ranier, Joel E.; Reeves, Alice A.; Caskey, C. Thomas

LOCATION: Inst. Mol. Genet., Baylor Coll. Med., Houston, TX, 77030, USA

JOURNAL: Science (Washington, D. C., 1883-) DATE: 1988 VOLUME: 239

NUMBER: 4846 PAGES: 1416-18 CODEN: SCIEAS ISSN: 0036-8075 LANGUAGE: English

SECTION:

CA203003 Biochemical Genetics

CA213XXX Mammalian Biochemistry

CA214XXX Mammalian Pathological Biochemistry

IDENTIFIERS: Duchenne muscular dystrophy gene muscle brain, mRNA Duchenne muscular dystrophy mouse

DESCRIPTORS:

Brain, metabolism... Muscle, metabolism...

Duchenne muscular dystrophy gene expression, of mouse, mental retardation of human in relation to

Duchenne muscular dystrophy gene of, expression in muscle and brain of,
mental retardation in human in relation to
Ribonucleic acid formation, messenger...
Duchenne muscular dystrophy-related, in muscle and brain of mouse,
mental retardation in human in relation to
Gene and Genetic element, animal, Dmd...
for Duchenne muscular dystrophy, expression of, in muscle and brain of
mouse, mental retardation in human in relation to
Muscular dystrophy, Duchenne...
gene Dmd for, muscle and brain of mouse expression of, mental
retardation in human in relation to

6/7/3 (Item 1 from file: 5)
0019124485 BIOSIS Number: 87059138
DELETION SCREENING OF THE DUCHENNE MUSCULAR DYSTROPHY LOCUS VIA MULTIPLEX
DNA AMPLIFICATION
CHAMBERLAIN J

t 6/7/3-9

6/7/3 (Item 1 from file: 5)
0019124485 BIOSIS Number: 87059138
DELETION SCREENING OF THE DUCHENNE MUSCULAR DYSTROPHY LOCUS VIA MULTIPLEX
DNA AMPLIFICATION
CHAMBERLAIN J S; GIBBS R A; RANIER J E; NGUYEN P N; CASKEY C T
INST. MOL. GENET., BAYLOR COLL. MED., HOUSTON, TEX. 77030, USA.
NUCLEIC ACIDS RES 16 (23). 1988. 11141-11156. CODEN: NARHA
Language: ENGLISH

The application of recombinant DNA technology to prenatal diagnosis of
many recessively inherited X-linked diseases is complicated by a high
frequency of heterogenous, new mutations (1). Partial gene deletions
account for more than 50% of Duchenne muscular dystrophy (DMD) lesions, and
approximately one-third of all cases result from a new mutation (2-5). We
report the isolation and DNA sequence of several deletion prone exons from
the human DMD gene. We also describe a rapid method capable of detecting
the majority of deletions in the DMD gene. This procedure utilizes
simultaneous genomic DNA amplification of multiple widely separated
sequences and should permit deletion scanning at any hemizygous locus. We
demonstrate the application of this multiplex reaction for prenatal and
postnatal diagnosis of DMD.

6/7/4 (Item 2 from file: 5)
0019056570 BIOSIS Number: 26033887
RAPID DETECTION OF DELETIONS AT THE DUCHENNE MUSCULAR DYSTROPHY LOCUS VIA
MULTIPLEX GENOMIC DNA AMPLIFICATION
CHAMBERLAIN J S; GIBBS R A; RANIER J E; NGUYEN P N; FARWELL N J; CASKEY C
T
INST. MOLECULAR GENETICS, BAYLOR COLL. MED., HOUSTON, TEX.
30TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, NEW
ORLEANS, LOUISIANA, USA, OCTOBER 12-15, 1990. AM J HUM GENET 43 (3
SUPPL.). 1990. A178. CODEN: AJHG
Language: ENGLISH

6/7/5 (Item 3 from file: 5)
0010595390 BIOSIS Number: 35050990

EXPRESSION OF THE MURINE DUCHENNE MUSCULAR DYSTROPHY GENE IN THE MUSCLE
AND BRAIN OF NORMAL AND MUTANT MDX MICE
CHAMBERLAIN J S; PEARLMAN J A; GIBBS R A; RANIER J E; FARWELL N J; CASKEY
C T

INST. MOL. GENET., HOWARD HUGHES MED. INST., BAYLOR COLL. MED., HOUSTON,
TX. 77030, USA.

MEETING ON CELLULAR AND MOLECULAR BIOLOGY OF MUSCLE DEVELOPMENT HELD AT
THE UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIUM ON MOLECULAR AND
CELLULAR BIOLOGY, FEBRUARY 28-APRIL 10, 1988. J CELL BIOCHEM SUPPL 0 (12
PART C). 1988. 370. CODEN: JCBSD

Language: ENGLISH

6/7/8 (Item 4 from file: 5)

001675020 BIOSIS Number: 35050818

EXPRESSION OF THE MURINE DUCHENNE MUSCULAR DYSTROPHY GENE IN THE MUSCLE
AND BRAIN OF NORMAL AND MUTANT MDX MICE

CHAMBERLAIN J S; PEARLMAN J A; GIBBS R A; RANIER J E; FARWELL N J; CASKEY
C T

INST. MOL. GENET., HOWARD HUGHES MED. INST., BAYLOR COLL. MED., HOUSTON,
TX. 77030.

MEETING ON CELLULAR AND MOLECULAR BIOLOGY OF MUSCLE DEVELOPMENT HELD AT
THE UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIUM ON MOLECULAR AND
CELLULAR BIOLOGY, FEBRUARY 28-APRIL 10, 1988. J CELL BIOCHEM SUPPL 0 (12
PART C). 1988. 319. CODEN: JCBSD

Language: ENGLISH

6/7/7 (Item 5 from file: 5)

0016250436 BIOSIS Number: 85121651

EXPRESSION OF THE MURINE DUCHENNE MUSCULAR DYSTROPHY GENE IN MUSCLE AND
BRAIN

CHAMBERLAIN J S; PEARLMAN J A; MUZY D M; GIBBS R A; RANIER J E; REEVES A
A; CASKEY C T

INST. MOLECULAR GENETICS, BAYLOR COLL. MED., ONE BAYLOR PLAZA, HOUSTON,
TX 77030.

SCIENCE (WASH D C) 239 (4846). 1988. 1416-1418. CODEN: SCIEA

Language: ENGLISH

Complementary DNA clones were isolated that represent the 5' terminal 2.5
kilobases of the murine Duchenne muscular dystrophy (Dmd) messenger RNA
(mRNA). Mouse Dmd mRNA was detectable in skeletal and cardiac muscle and at
a level approximately 90 percent lower in brain. Dmd mRNA is also present,
but at much lower than normal levels, in both the muscle and brain of three
different strains of dystrophic mdx mice. The identification of Dmd mRNA in
brain raises the possibility of a relation between human Duchenne muscular
dystrophy (DMD) gene expression and the mental retardation found in some
DMD males. These results also provide evidence that the mdx mutations are
allelic variants of mouse Dmd gene mutations.

6/7/8 (Item 1 from file: 155)

06781552 89083552

Deletion screening of the Duchenne muscular dystrophy locus via multiplex
DNA amplification.

Chamberlain JS; Gibbs RA; Ranier JE; Nguyen PN; Caskey CT

Institute for Molecular Genetics, Baylor College of Medicine, Houston, TX
77030.

Nucleic Acids Res (ENGLAND) Dec 9 1988, 16 (23) p11141-53, ISSN
0305-1048 Journal Code: OBL

Language: ENGLISH

The application of recombinant DNA technology to prenatal diagnosis of
many recessively inherited X-linked diseases is complicated by a high
frequency of heterogeneous, new mutations (1). Partial gene deletions
account for more than 50% of Duchenne muscular dystrophy (DMD) lesions, and
approximately one-third of all cases result from a new mutation (2-5). We
report the isolation and DNA sequence of several deletion prone exons from
the human DMD gene. We also describe a rapid method capable of detecting
the majority of deletions in the DMD gene. This procedure utilizes
simultaneous genomic DNA amplification of multiple widely separated

sequences and should permit deletion scanning at any hemizygous locus. We demonstrate the application of this multi-probe reaction for prenatal and postnatal diagnosis of DMD.

6/7/92 (Item 2 from file: 155)

04511022 83139232

Exon 5 of the murine Duchenne muscular dystrophy gene in muscle and brain.

Chamberlain JS; Pearson JA; Muzny DM; Gibbs RA; Ranier JE; Caskey CT; Reeves AP

Institute for Molecular Genetics, Baylor College of Medicine, Houston, TX 77030.

Science Mar 18 1988; 239 (4846) p1416-8, ISSN 0036-8075

Journal Code: UJ7

Language: ENGLISH

Complementary DNA clones were isolated that represent the 5' terminal 2.5 kilobases of the murine Duchenne muscular dystrophy (Dmd) messenger RNA (mRNA). Mouse Dmd mRNA was detectable in skeletal and cardiac muscle and at a level approximately 90 percent lower in brain. Dmd mRNA is also present, but at much lower than normal levels, in both the muscle and brain of three different strains of dystrophic mdx mice. The identification of Dmd mRNA in brain raises the possibility of a relation between human Duchenne muscular dystrophy (DMD) gene expression and the mental retardation found in some DMD cases. These results also provide evidence that the mdx mutations are allelic variants of mouse Dmd gene mutations.

??t s14/7/1-13

14/7/1 (Item 1 from file: 5)

0010300025 BIOSIS Number: 76087517

DELETION AND AMPLIFICATION OF THE HYPO XANTHINE GUANINE PHOSPHO RIBOSYL TRANSFERASE EC-2.4.2.3 LOCUS IN CHINESE HAMSTER CELLS

FUSCOE J C; FENWICK R S JR; LEDBETTER D H; CASKEY C T

DEPT. MED., BAYLOR COLL. MED., HOUSTON, TEX. 77030.

MOL CELL BIOL 3 (4). 1983. 1006-1096. CODEN: MCEBD

Language: ENGLISH

Somatic cell selective techniques and hybridization analyses with a cloned cDNA probe were used to isolate and identify Chinese hamster cell lines in which the X-linked gene for hypoxanthine-guanine phosphoribosyltransferase (HGPRT) were altered. Two of 19 HGPRT-deficient mutants selected had major DNA deletions affecting the HGPRT locus. Cytogenetic studies revealed that the X chromosome of each deletion mutant had undergone a translocation event, whereas those from the remaining 17 mutants were normal. Phenotypic revertants of the thermosensitive HGPRT mutant RJK526 were isolated, and amplification of the mutant allele was shown to be the predominant mechanism of reversion. Comparisons of restriction enzyme fragments of DNA for deletion vs. amplification strains identified two regions of the Chinese hamster genome that contained homology to the cDNA probe. One was much larger than the 1600-nucleotide mRNA for HGPRT and to be comprised of linked fragments that contained the functional HGPRT gene. The 2nd was neither transcribed nor tightly linked to the functional gene. These initial studies of HGPRT alterations at the level of DNA, thus identified molecular mechanisms of phenotypic variation.

??t s15/7/1-12

15/7/1 (Item 1 from file: 5)

0018080315 BIOSIS Number: 05087084

REGIONAL LOCALIZATION OF THE MURINE DUCHENNE MUSCULAR DYSTROPHY GENE ON THE MOUSE X CHROMOSOME

CHAMBERLAIN J S; GRANT S C; REEVES A A; MULLINS L J; STEPHENSON D A;

HOFFMAN E P; MONACO A P; KUNKEL L B; CASKEY C T; CHAPMAN V M

INST. MOL. GENET., BAYLOR COLL. MED., ONE BAYLOR PLAZA, HOUSTON, TEX.

77030.

SOMATIC CELL MOL GENET 10 (4). 1987. 671-673. CODEN: SCYGD

Language: ENGLISH

The murine locus corresponding to the human Duchenne/Becker muscular dystrophy (DMD) gene has been regionally mapped on the mouse X chromosome

by hybridizing DNA from transgenic mouse crosses with a cDNA clone for the mouse Dmd gene. The results demonstrate that the relative organization of genes on the murine and human X chromosomes is more divergent than has previously been postulated. Furthermore, the mouse Dmd gene maps to a similar region of the X chromosome as does the mouse muscular dystrophy mutation mdx, providing further evidence that the mdx mutant may be a murine equivalent of human DMD. However, Southern analysis of portions of the mouse Dmd gene has not yet revealed any differences between mdx and wild type mice.

15/7/82 (Item 2 from file: 5)
0017101741 BIOSIS Number: 84045692

ISOLATION OF COMPLEMENTARY DNA CLONES FOR THE CATALYTIC GAMMA SUBUNIT OF MOUSE MUSCLE PHOSPHORYLASE KINASE EXPRESSION OF MESSENGER RNA IN NORMAL AND MUTANT PHK MICE

CHAMBERLAIN J S; VANTUINEN P; REEVES A A; PHILIP B A; CASKEY C T
INST. MOL. GENET., DAVLOR COLL. MED., HOUSTON, TEX. 77030, USA.
PROC NATL ACAD SCI U S A 84 (9), 1987, 2886-2890. CODEN: PNASA
Language: ENGLISH

We have isolated and characterized cDNA clones for the gamma subunit of mouse muscle phosphorylase kinase (gamma-Phk). These clones were isolated from a lambda.gtlI mouse muscle cDNA library via screening with a synthetic oligonucleotide probe corresponding to a portion of the rabbit gamma-Phk amino acid sequence. The gamma-Phk cDNA clones code for a 337-amino acid protein that shares 93% amino acid sequence identity with the corresponding rabbit amino acid sequence. RNA gel blot analysis reveals that the muscle gamma-Phk probe hybridizes to two mRNA species (2.4 and 1.6 kilobases) in skeletal muscle, cardiac muscle, and brain, but does not hybridize to liver RNA. Phk-deficient I-strain (Phk) mouse muscle contains reduced levels of gamma-Phk mRNA as compared with control mice. Although the Phk defect is an X-linked recessive trait, hybridization to a human-mouse somatic cell hybrid mapping panel shows that the gamma-Phk gene is not located on the X chromosome. Rather, the gamma-Phk cross-hybridizing human restriction fragments map to human chromosomes 7 (multiple) and 11 (single). Reduced gamma-Phk mRNA in I-strain mice, therefore, appears to be a consequence of the Phk-mutant trait and does not stem from a mutant gamma-subunit gene.

15/7/82 (Item 3 from file: 5)
0016632669 BIOSIS Number: 82062841

THE 5' FLANKING REGION OF THE ORNITHINE TRANSCARBAMYLASE GENE CONTAINS DNA SEQUENCES REGULATING TISSUE-SPECIFIC EXPRESSION

VERES G; CRAIGEN W J; CASKEY C T
HUNGARIAN ACAD. SCI., BIOL. RES. CENT., 6701 SZEGED P.O. BOX 521,
HUNGARY.

J BIOL CHEM 261 (17), 1986, 7508-7591. CODEN: JBCHA
Language: ENGLISH

Ornithine transcarbamylase (OTCase) is a mitochondrial matrix enzyme that catalyzes the 2nd step in the mammalian urea cycle. The gene encoding OTCase is located on the X chromosome and expression of OTCase is limited almost exclusively to hepatocytes. We have characterized a lambda. phage recombinant, isolated from a mouse genomic library, that spans the first two exons of the mouse OTCase gene. Nuclease S1 mapping and primer extension analysis of this clone allowed us to determine that the transcription start site is 136 base pairs (bp) upstream from the translation initiation codon. Two TATA-like sequences were found 25 and 153 bp from the transcription initiation point. An 800-bp fragment containing the 5' flanking region of the OTCase gene was fused upstream to the coding sequence of the chloramphenicol acetyltransferase gene to assay promoter activity. This plasmid was introduced into mouse fibroblast NIH 3T3 cells and human hepatoma Hep G2 cells by the calcium phosphate co-precipitation method. After DNA transfection chloramphenicol acetyltransferase activity was observed only in Hep G2 cells. We conclude that this 800-bp fragment contains sufficient information for control of OTCase gene expression in a tissue-specific manner, probably by interacting with tissue-acting factor(s) which are present in the other cell lines.

15/17/84 (11) 5 44 1 501 1 51

001900000 BINGO M 1 1 1 78040001

ORGANIZATION OF THE HYPOXANTHINE-GUANINE PHOSPHORIBOSYLTRANSFERASE GENE AND RELATED SEQUENCES IN THE HUMAN GENOME

BAILEY D J, HARRISON D J, STANFORD D E, LEBETTER D W, CASKEY C T, CHINSAULT A C

HOUSTON MEMORIAL HEP. INST. LAB., BAYLOR COLL. OF MED., HOUSTON, TEX. 77030.

GENOTYPE AND NO. GENES 10 (1) 1984. 400-404. CODEN: SCMD

Lang: ENGLISH

Comp. with 81.4% homology. Distribution of complementary DNA probes to DNA from cells carrying either 1 or 2 H chromosomes was used to distinguish sequences derived from the functional locus for hypoxanthine-guanine phosphoribosyltransferase (HPRT) on the X chromosome from 4 independent HPRT-like autosomal sequences in the human genome. Subfragments of cDNA were then used to orient fragments from the HPRT locus with respect to the cDNA sequence. The chromosomal origin of each of the autosomal sequences was determined by Southern analysis using DNA from a panel of human-Chinese hamster fibroblast cell hybrids. Two of the HPRT-like sequences were localized to chromosomes 11, the 3rd to chromosome 2, and the 4th to the region between p18 and q11 on chromosome 5. Three of these 4 autosomal sequences were isolated from genomic recombinant libraries and subcloned fragments from each were then used as probes to study restriction fragment length polymorphisms (RFLP) at other loci. A RFLP for MspI was found at the HPRT-like locus on chromosome 5 with a 1.8 kb [kilobase] major allele (frequency = 0.8) and a 0.6 kb minor allele (frequency = 0.2).

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15/17/84 (11) 5 44 1 501 1 51

001900000 BINGO M 1 1 1 78075000

AMPLIFICATION AND MUTATION AS A MECHANISM FOR REVERSION OF AN HPRT MUTATION

RENNICK D A JR, SUGGS J G, CASKEY C T

ST. JOSEPH'S HOSPITAL, HALIFAX, NOVA SCOTIA, CANADA B3H 4H7.

GENOTYPE AND NO. GENES 10 (1) 1984. 71-84. CODEN: SCMD

Lang: ENGLISH

Complementary DNA was used for hypoxanthine-guanine phosphoribosyltransferase (HPRT) to analyze the HPRT gene and mRNA in an HPRT deficient mutant of Chinese hamster cells (RJK10) and its HPRT positive revertants. By Southern blot analysis, no DNA rearrangements were detected within the genes from any of the cell lines examined. Four of 7 spontaneous revertants each contained 10- to 20-fold more copies of the HPRT gene than did RJK10 or wild-type cells. The gene was not amplified in 4 mitogen-induced revertants. The RJK10 mutation did not alter the size or concentration of HPRT mRNA and representatives of the revertants contained the mRNA in amounts proportional to the number of genes they carried. Examples of clones with either stable or unstable gene amplification were identified and their HPRT-positive phenotypes were shown to be dependent on the gene amplification. In a stably amplified revertant, the extra genes were found to be syntenic with the X chromosome marker glucose-6-phosphate dehydrogenase. In an unstable revertant only one of the 10-20 copies of the gene could be shown to be syntenic with RJK10 or revert by at least 2 distinct mechanisms: a 1.1 kb deletion of the HPRT gene, which occurred spontaneously, or point mutation, which followed after exposure to mutagens.

X

15/17/84 (11) 5 44 1 501 1 51

001900000 BINGO M 1 1 1 78040001

STRUCTURE EXPRESSION AND MUTATION OF THE HYPO XANTHINE PHOSPHO RIBOSYL TRANSFERASE EC 2.4.2.8 GENE

MELTON D W, KOSICKI D G, BRENNAN J, CASKEY C T

DEPT. MOLEC. BIOL., KING'S BUILD., UNIV. EDINBURGH, EDINBURGH EH9 3JR, UK.

PROG NATL ACAD SCI U S A 81 (7) 1984. 2147-2151. CODEN: PNAS

Lang: ENGLISH

The complementary DNA for hypoxanthine phosphoribosyltransferase (HPRT; EC 2.4.2.8) gene was isolated from a human cell line and its structure was determined. This X

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One of the two genes is > 33 kilobases long and is split into 9 exons. The other gene is 1.5 kb long and contains 3 exons. The exon-intron boundaries were determined, and a single-base substitution in the HPRT cDNA sequence was identified. A cDNA sequence from a mouse neuroblastoma cell line was found to encode a normal HPRT protein. The 5' end of the gene was defined, both by nuclease S1 protection and primer extension analysis, and by a functional assay in which an HPRT minigene, capable of expression in cultured cells, was created by ligating the 5' end of the gene to the wild-type human HPRT cDNA. Sequences normally associated with eukaryotic promoters are not present in the immediate 5'-flanking region of the HPRT gene, which is instead highly G+C rich. This observation is discussed in relation to the possible link between DNA methylation and X-chromosome inactivation.

15/7/77 (Item 7 from file: 5)

0014242259 BIOSIS Number: 77075243

A 3 ALLELE RESTRICTION FRAGMENT LENGTH POLYMORPHISM AT THE HYPO XANTHINE PHOSPHO RIBOSYL TRANSFERASE EC-2.1.2.3 LOCUS IN MAN

MUGGERDAUM R L; CROWDER W E; MYHRE W L; CASKEY C T

HOWARD HUGHES MED. INSTITUTE LAB., DEP. MED., BAYLOR COLL. MED., HOUSTON, TEX. 77030.

PROC NATL ACAD SCI U S A 80 (13). 1983. 4035-4039. CODEN: PNASA

Language: ENGLISH

Using cloned cDNA (complementary DNA) sequences of murine and human hypoxanthine phosphoribosyltransferase (HPRT; IMP:pyrophosphate phosphotransferase, EC 2.4.2.8), a 3-allele restriction-fragment-length polymorphism for the restriction endonuclease BamHI at the human HPRT locus was characterized and identified. The alleles are expressed phenotypically on Southern blots as 2 distinct pairs of fragments that hybridize to HPRT cDNA: a 22-kilobase (kb)/25-kb pair; a 12-kb/25-kb pair; and a 22-kb/18-kb pair. In addition to fragments from the HPRT locus, sequences recognized by both HPRT cDNA probes are also present on at least 2 autosomes in the human genome. Allele frequencies in an unselected Caucasian population are 0.77 for the 22-kb/25-kb allele, 0.16 for the 12-kb/25-kb allele, and 0.07 for the 22-kb/18-kb allele, resulting in an average heterozygosity of 36% in females in this population. This polymorphism should facilitate gene mapping by linkage in this region of the human X chromosome.

15/7/78 (Item 1 from file: 155)

00761035 89030045

Rapid and precise mapping of the Escherichia coli release factor genes by two physical approaches.

Lee CG; Kohara Y; Akiyama K; Smith CL; Craigie MJ; Caskey CT

Institute for Molecular Genetics, Baylor College of Medicine, Houston, Texas 77030.

J. Molecular Biology (UNITED STATES) Oct 1989, 170 (10) p4537-41, ISSN 0021-9193 Journal Code: HH3

Contract/Grant No.: GM34438

Language: ENGLISH

The termination of protein synthesis in Escherichia coli requires two codon-specific factors termed RF1 and RF2. RF1 mediates UAA- and UAG-directed termination, while RF2 mediates UAA- and UGA-directed termination. The genes encoding these factors have been isolated and sequenced, and RF2 was found to be encoded in two separate reading frames. The map position of RF1 has been reported as 27 min on the E. coli chromosome, while the RF2 map position has not yet been identified. In this study, two new and independent methods for gene mapping, using pulsed field gel electrophoresis and an ordered bacteriophage library spanning the entire chromosome, were used to localize the map position of the RF2 gene. In addition, the location of the RF1 gene was more precisely defined. The RF2 gene is located at 62.3 min on the chromosome, while the RF1 gene is located at 26.7 min. This approach to mapping cloned genes promises to be a rapid and simple means for determining the gene order of the genome.

15/7/78 (Item 2 from file: 155)

00761035 89103721

The function, structure and regulation of E. coli peptide chain release factors.

Craig MJ, Caskey CT

Houston Hughes Medical Institute, Baylor College of Medicine, Houston, TX 77030.

Biochim Biophys Acta (FRANCE) Oct 1987, 69 (10) p1031-41, ISSN 0304-4199

Journal Code: A14

Contract/Grant No.: GM34430; GM07030

Language: ENGLISH

Document Type: Review

The termination of protein synthesis in Escherichia coli depends upon the soluble protein factors RF1 or RF2. RF1 catalyzes UAG and UAA dependent termination, while RF2 catalyzes UGA and UAA dependent termination. The proteins have been purified to homogeneity, their respective genes isolated, and their primary structures deduced from the DNA sequences. The sequences reveal considerable conserved homology, presumably reflecting functional similarities and a common ancestral origin. The RFs are encoded as single copy genes on the bacterial chromosome. RF2 exhibits autogenous regulation in an in vitro translation system. The mechanism of autoregulation appears to be an in-frame UGA stop codon that requires a 1+ frameshift for the continued synthesis of the protein. Frameshifting prior to the inframe stop codon occurs at a remarkably high frequency by an unknown mechanism. Future studies will be directed at understanding how RFs interact with the ribosomal components, and further defining the mechanism of RF2 frameshifting. (43 Refs.)

15/7/10 (Item 3 from file: 155)

05922027 86224037

The 5' flanking region of the ornithine transcarbamylase gene contains DNA sequences regulating tissue-specific expression.

Veres G; Craig MJ; Caskey CT

J Biol Chem Jun 15 1995, 261 (17) p7523-31, ISSN 0021-9259

Journal Code: HIV

Contract/Grant No.: GM07030

Language: ENGLISH

Ornithine transcarbamylase (OTCase) is a mitochondrial matrix enzyme that catalyzes the 2nd step in the mammalian urea cycle. The gene encoding OTCase is located on the X chromosome and expression of OTCase is limited almost exclusively to hepatocytes. We have characterized a lambda phage recombinant, isolated from a mouse genomic library, that spans the first two exons of the mouse OTCase gene. Nuclease S1 mapping and primer extension analysis of this clone allowed us to determine that the transcription start site is 135 base pairs (bp) upstream from the translation initiation codon. Two TATA-like sequences were found 25 and 153 bp from the transcription initiation point. An 800-bp fragment containing the 5' flanking region of the OTCase gene was fused upstream to the coding sequence of the chloramphenicol acetyltransferase gene to assay promoter activity. This plasmid was introduced into mouse fibroblast NIH 3T3 cells and human hepatoma Hep G2 cells by the calcium phosphate co-precipitation method. After DNA transfection chloramphenicol acetyltransferase activity was observed only in Hep G2 cells. We conclude that this 800-bp fragment contains sufficient information to control OTCase gene expression in a tissue-specific manner, probably by interacting with trans-acting factor(s) which are not present in the other cell line.

15/7/11 (Item 4 from file: 155)

05269967 84193067

Structure, expression, and mutation of the hypoxanthine phosphoribosyltransferase gene.

Melton DW; Konecki DS; Brannan J; Caskey CT

Proc Natl Acad Sci U S A Apr 1984, 81 (7) p2147-51, ISSN 0027-8424

Journal Code: PV3

Contract/Grant No.: AMS1428-01

Language: ENGLISH

The wild-type mouse hypoxanthine phosphoribosyltransferase (HPRT; EC 2.4.2.8) gene has been

Isolated from genomic libraries and its structure has been determined. This X-chromosome-linked gene is greater than 83 kilobases long and is split into nine exons. All the exon sequences have been determined, and a single-base substitution in the HPRT cDNA coding sequence from a mouse neuroblastoma cell line that overproduces a mutant HPRT protein has been identified. The 5' end of the gene has been defined, both by nuclease S1 protection and primer extension studies and by a functional assay in which an HPRT minigene, capable of expression in cultured cells, was created by ligating the 5' end of the gene onto wild-type human HPRT cDNA. Sequences normally associated with eukaryotic promoters are not present in the immediate 5'-flanking region of the HPRT gene, which is instead highly G+C rich. This observation is discussed in relation to the possible link between DNA methylation and X-chromosome inactivation.

15/7/12 (Item 1 from file: 357)

073726 DBA Accession No.: 82-04525

The genetic structure of mouse ornithine-transcarbamylase - mapping and DNA sequence determination of ornithine- carbamyltransferase

AUTHOR: Schaller S E; Vozar G; Caskey C T

CORPORATE SOURCE: Institute for Molecular Genetics, Howard Hughes Medical Institute, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX 77030, USA.

JOURNAL: Nucleic Acids Res. (16, 4, 1593-601) CODEN: NARHAD

PUBLICATION YEAR: 1988 LANGUAGE: English

ABSTRACT: The gene encoding the mouse urea cycle enzyme, ornithine-transcarbamylase (OTC, EC-2.1.3.3, ornithine- carbamyltransferase) has been isolated and characterized. A mouse genomic DNA library was constructed as a partial HaeIII digestion of C57BL/6J mouse DNA cloned into phage Charon 1A with EcoRI linkers and plated on Y1089 host. Plaque hybridization was performed using a variety of cDNA probes for mouse OTC. Restriction mapping of the clones was carried out using the rapid cut-site technique, and restriction fragments from phage clone inserts were sequenced by the dideoxy-nucleotide chain termination method after ligation with pUC8 and pUC9 and phage M13 sequencing phage and transformation into competent TC-1 or DH-5-lpha bacteria. The OTC gene was localized on 5 partially overlapping phage lambda clones. It is split between 10 exons distributed over approximately 70 kb of the X chromosome. The introns are 38 bases to 26 kb in length, while the donor/splice acceptor sequences conform to the consensus of other eukaryotic genes. (22 ref)

?t s23/7/1-23

23/7/1 (Item 1 from file: 399)

109001825 CA: 109(11)825d JOURNAL:

Antisense RNA inhibition of endogenous genes

AUTHOR(S): Stout, J. Timothy; Caskey, C. Thomas

LOCATION: Inst. Mol. Genet., Baylor Coll. Med., Houston, TX, 77030, USA

JOURNAL: Methods Enzymol. DATE: 1997 VOLUME: 151 NUMBER: Mol. Genet.

Mamm. Cells PAGES: 510-50 CODEN: MENZAU ISSN: 0076-6879 LANGUAGE: English

SECTION:

CA263035 Biochemical Genetics

CA2144XX Mammalian Pathological Biochemistry

IDENTIFIERS: ornithine RNA hypoxanthine phosphoribosyltransferase deficiency

DESCRIPTION:

Gene and Cell: 109(11)825d

Antisense RNA inhibition of endogenous

RNA: 109(11)825d, RNA: 109(11)825d, RNA: 109(11)825d

Antisense RNA inhibition of

Antisense RNA inhibition of

CA263035 Biochemical Genetics

23/7/1 (Item 1 from file: 399)

109001825 CA: 109(11)825d JOURNAL:

Antisense RNA inhibition of endogenous genes

1. 23/7/83 (Item 1 from file: 5)
0010071590 BIOSIS Number: 36033909
DIRECT DNA SEQUENCE ANALYSIS OF IN-VITRO AMPLIFIED HPRT COMPLEMENTARY DNA
FROM LEUKAEMIC PATIENTS
GIBBS B A, NGUYEN P N, CASKEY C T
MOL. MOLECULAR GENETICS, BAYLOR COLL. MED., HOUSTON, TEXAS.
38TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, NEW
ORLEANS, LOUISIANA, USA, OCTOBER 12-15, 1988. AM J HUM GENET 43 (3
SUPPL.), 1988. A184. CODEN: AJHG8A
Language: ENGLISH

2. 23/7/83 (Item 2 from file: 5)
0010051540 BIOSIS Number: 36033677
A COMPARISON OF INTRAGENIC DELETIONS BETWEEN DUCHENNE AND BECKER MUSCULAR
DYSTROPHY PATIENTS
BAUMBACH L L, HARD P A, CHAMBERLAIN J S, CASKEY C T
MOL. MOLECULAR GENETICS, BAYLOR COLL. MED., HOUSTON, TEX.
38TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, NEW
ORLEANS, LOUISIANA, USA, OCTOBER 12-15, 1988. AM J HUM GENET 43 (3
SUPPL.), 1988. A176. CODEN: AJHG8A
Language: ENGLISH

3. 23/7/83 (Item 3 from file: 5)
0010056240 BIOSIS Number: 36033563
CHARACTERIZATION OF PATIENTS WITH GLYCEROL KINASE DEFICIENCY GKD
UTILIZING COMPLEMENTARY DNA PROBES FOR THE DUCHENNE MUSCULAR DYSTROPHY DMD
LOCUS
TINSIN J A, WU D, CHAMBERLAIN J, BAUMBACH L, LARSEN P, SELTZER W K,
NECKES E R
BAYLOR COLL. MED., HOUSTON, TEX.
38TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, NEW
ORLEANS, LOUISIANA, USA, OCTOBER 12-15, 1988. AM J HUM GENET 43 (3
SUPPL.), 1988. A97. CODEN: AJHG8A
Language: ENGLISH

4. 23/7/83 (Item 4 from file: 5)
001003034 BIOSIS Number: 36036934
THE ISOLATION AND CHARACTERIZATION OF A PORCINE COMPLEMENTARY DNA FOR
URATE OXIDASE AND PHOSPHORIBOSYLPHOSPHATE SYNTHETASE
LEE C C, NIKOLAKOPOULOS G, GIBBS B A, NGUYEN P N, CASKEY C T

5. 23/7/83 (Item 5 from file: 5)
001003034 BIOSIS Number: 36036934
THE ISOLATION AND CHARACTERIZATION OF A PORCINE COMPLEMENTARY DNA FOR
URATE OXIDASE AND PHOSPHORIBOSYLPHOSPHATE SYNTHETASE
LEE C C, NIKOLAKOPOULOS G, GIBBS B A, NGUYEN P N, CASKEY C T

6. 23/7/83 (Item 6 from file: 5)
001003034 BIOSIS Number: 36036934
THE ISOLATION AND CHARACTERIZATION OF A PORCINE COMPLEMENTARY DNA FOR
URATE OXIDASE AND PHOSPHORIBOSYLPHOSPHATE SYNTHETASE
LEE C C, NIKOLAKOPOULOS G, GIBBS B A, NGUYEN P N, CASKEY C T

INST. MOL. GENET., BAYLOR COLL. MED., HOUSTON, TEX. 77030, USA.
III INTERNATIONAL SYMPOSIUM ON HUMAN PURINE AND PYRIMIDINE METABOLISM,
KYOTO, JAPAN, JULY 17-21, 1988. PEDIATR RES 24 (1). 1988. 124.
CODEN: PEDIRE
Language: ENGLISH

22/7/87 (Item 5 from file: 5)
0012074312 BIOSIS Number: 34031232
ORNITHINE TRANSCARBAMYLASE GENE STRUCTURE AND THE IDENTIFICATION OF A
POINT MUTATION RESPONSIBLE FOR OTC-DEFICIENCY IN THE SPARSE FUR MOUSE
CHAMBERLAIN J G; VERES G; GIBBS R A; CASKEY C T
INST. MOLECULAR GENETICS, BAYLOR COLL. MED., HOUSTON, TEX.
80TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, SAN DIEGO,
CALIFORNIA, USA, OCTOBER 7-10, 1987. AM J HUM GENET 41 (3 SUPPL.). 1987.
CODEN: AJHGDA
Language: ENGLISH

22/7/87 (Item 6 from file: 5)
0012054102 BIOSIS Number: 34031151
ISOLATION OF A COMPLEMENTARY DNA CLONE TO THE MOUSE EQUIVALENT OF THE
DUCHENNE MUSCULAR DYSTROPHY GENE
CHAMBERLAIN J G; REEVES A A; MUZNY D M; CASKEY C T
HOWARD HUGHES MED. INST., BAYLOR COLL. MED., HOUSTON, TEX.
88TH ANNUAL MEETING OF THE AMERICAN SOCIETY OF HUMAN GENETICS, SAN DIEGO,
CALIFORNIA, USA, OCTOBER 7-10, 1987. AM J HUM GENET 41 (3 SUPPL.). 1987.
CODEN: AJHGDA
Language: ENGLISH

22/7/89 (Item 7 from file: 5)
0017343292 BIOSIS Number: 84066499
THE MOLECULAR BASIS OF THE SPARSE FUR MOUSE MUTATION
VERES G; GIBBS R A; SCHERER S E; CASKEY C T
INST. MOL. GENETICS, HOWARD HUGHES MED. INST., BAYLOR COLL. MED.,
HOUSTON, TEX. 77030.
SCIENCE (WASH D C) 237 (4813). 1987. 415-417. CODEN: SCIEA
Language: ENGLISH
The ornithine transcarbamylase-deficient sparse fur mouse is an excellent
model to study the most common human urea cycle disorder. The mutation has
been well characterized by both biochemical and enzymological methods, but
its exact nature has not been revealed. A single base substitution in the
complementary DNA for ornithine transcarbamylase from the sparse fur mouse
has been identified by means of a combination of two recently described
techniques for rapid mutational analysis. This strategy is simpler than
conventional complementary DNA library construction, screening, and
sequencing, which has often been used to find a new mutation. The ornithine
transcarbamylase gene in the sparse fur mouse contains a C to A
transversion that alters a histidine residue to asparagine residue at amino
acid 117.

22/7/89 (Item 8 from file: 5)
0017177757 BIOSIS Number: 89035631
CONSTRUCTION OF A DEFECTIVE RETROVIRUS CONTAINING THE HUMAN HYPOXANTHINE
PHOSPHORIBOSYLTRANSFERASE COMPLEMENTARY DNA AND ITS EXPRESSION IN CULTURED
CELLS AND MOUSE EMBRYO
CHANG S M M; LAGER-SMITH K; TSAO T Y; HENKEL-TIGGES J; VAISHNAV S; CASKEY
C T
HOWARD HUGHES MED. INST., INST. MOLECULAR GENETICS, BAYLOR COLLEGE MED.,
HOUSTON, TEXAS 77030.
MOL CELL BIOL 7 (2). 1987. 854-863. CODEN: MCEBD
Language: ENGLISH

Defective autotropic and amphotropic retroviral vectors containing the
cDNA for human hypoxanthine phosphoribosyltransferase (HPRT) were developed
for efficient gene transfer and high-level cellular expression of HPRT.
Helper cell clones which produced a high titer were generated by a
simplified method which minimizes cell culture. We used the pZIP-NcoSV(X)
vector containing a 1.0 kb HPRT cDNA. Viral titers of 10⁶ to 5

titers, 104/mt) of defective SVX HPRT B, a vector containing both the hprt and neo genes, were increased 2- to 12-fold by cocultivation of the protropic psi.2 and amphotropic PA-12 helper cells. Higher viral titers (8 times, 105 to 7.5 times, 106) were obtained when nonproducer NIH 3T3 cells or psi.2 and amphotropic PA-12 helper cells. Higher viral titers (8 times, 105 to 7.5 times, 106) were obtained when nonproducer NIH 3T3 cells or psi.2 cells carrying a single copy of SVX HPRT B were either transfected or infected by Moloney leukemia virus. The SVX HPRT B defective virus partially corrected the HPRT deficiency (4 to 50% of normal) of cultured normal and Lesh-Nyhan cells. However, instability of HPRT expression was detected in several infected clones. In these unstable variants, both retention and loss of the SVX HPRT B sequences were observed. In the former category, cells which became HPRT- (6-thioguanine resistant 6TG^r) also became 6410s, indicative of a cis-acting down regulation of expression. Both hypoxanthine-aminopterin-thymidine resistance (HAT^r) and 6410s could be regained by counterselection in hypoxanthine-aminopterin-thymidine. In vitro mouse bone marrow experiments indicated low-level expression of the neo gene in in vitro CFU assays. Individual CFU were isolated and pooled, and the human hprt gene was shown to be expressed. These studies demonstrated the applicability of vectors like SVX HPRT B for high-titer production of defective retroviruses required for hematopoietic gene transfer and expression.

23/7/11 (Item 9 from file: 5)

0016668192 BIOSIS Number: 01000000

5' REGULATORY ELEMENTS OF THE HUMAN HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE GENE

PATEL P J, TROSC T, CASKEY C T, CHINAULT A C

BAYLOR COLL. OF MED., HOUSTON, TX 77030.

SYMPOSIUM ON TRANSCRIPTIONAL CONTROL MECHANISMS HELD AT THE 15TH ANNUAL MEETING OF THE UCLA (UNIVERSITY OF CALIFORNIA-LOS ANGELES) SYMPOSIA ON MOLECULAR AND CELLULAR BIOLOGY, APR. 6-10, 1986. J CELL BIOCHEM SUPPL 0

(10 PART 2), 1986, 173. CODEN: JCBSD

Language: ENGLISH

23/7/12 (Item 10 from file: 5)

0016101557 BIOSIS Number: 01091970

FINE STRUCTURE OF THE HUMAN HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE GENE

PATEL P J, TROSC P C, CASKEY C T, CHINAULT A C

DEP. BIOCHEMISTRY, BAYLOR COLLEGE MED., HOUSTON, TEXAS 77030.

MOL CELL BIOL 6 (2), 1986, 393-403. CODEN: MCEBD

Language: ENGLISH

The human hypoxanthine phosphoribosyltransferase (HPRT) gene has been characterized by nucleic acid cloning, mapping, and DNA sequencing techniques. The entire gene, which is about 44 kilobases in length, is composed of nine exon elements. The positions of the introns within the coding sequence are identical to those of the previously characterized mouse HPRT gene, although there are significant differences between intron sizes for the two genes. HPRT minigenes have been used in a transient expression assay involving microinjection of TS rodent. The promoter of this gene resembles those of other recently characterized "housekeeping" genes in that it lacks CAAT- and TATA-like sequences, but contains several copies of the sequence CCGCCG. Both RNase protection and primer extension analysis indicate that human HPRT mRNA is heterogeneous at the 5' terminus, with transcription initiation occurring at sites located approx. 104 to approx. 169 base pairs upstream of the ATG codon. Comparison of the mouse and human HPRT 5' flanking sequences indicates that there are only limited stretches of shared sequence, although there are other shared features, such as an unusually high density of potential methylation sites, that may have evolved by divergence.

23/7/10 (Item 11 from file: 5)

001670000 BIOSIS Number: 00000013

EXPRESSION OF HUMAN AND MOUSE HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE MINIGENES

SHANK C M, TROSC T M, PATEL P J, CHINAULT A C, MELTON D M, CASKEY C T

RESEARCH CENTER FOR GENETICS, BAYLOR COLLEGE MED., HOUSTON, TX.
GENETIC METABOLISM, METABOLISM,
CAN DISCO, CALIF., 1984. "HY-20-103-1, 1985. PEDIAT. RES. 19 (7). 1985.
749. CODEN: PEDR
Language: ENGLISH

22/7/14 (Item 12 from 11/4/5)

0014266762 DISCO Number: 7300002

HYPXANTHINE GUANINE PHOSPHO RIBOSYL TRANSFERASE DETECTION OF A
MUTANT ALLELE BY RESTRICTION ENDE NUCLEASE ANALYSIS

WILSON J M, PROSSER E, NICHOLSON D L, CASKEY C T, KELLEY H N

DEPT. INTERNAL MED., UNIV. MICHIGAN MED. SCH., ANN ARBOR, MICH. 48109.

J CLIN INVEST. 72 (3), 1983. 767-770. CODEN: JCIN

Language: ENGLISH

A restriction enzyme developed for the direct analysis of a hypoxanthine-guanine phosphoribosyl transferase (HPRT) allele associated with a deficiency of hypoxanthine, and an early onset of gout. The functionally abnormal allele coded for by this mutant allele (HPRT-Toronto) differs from the normal allele by an arginine-to-glycine substitution at position 50. A single base change in the coding for arginine 50 can explain this substitution. Direct analysis of this point mutation is based on the recognition that it abolishes a Taq I recognition site in HPRT DNA. As expected, DNA from affected individuals with the HPRT-Toronto allele exhibited an abnormal restriction pattern when digested with Taq I and Taq I-Hinf II HPRT complementary DNAs: a normal 2.0-kb [kilobase] fragment is replaced by a 1.0 kb fragment. The 1.0/2.0-kb restriction fragment variation was used to detect the HPRT-Toronto allele in a heterozygote that was identified by the classical techniques used to diagnose classically the HPRT deficiency.

22/7/17 (Item 10 from 11/4/5)

0010002001 DISCO Number: 7300074

CLONED COMPLEMENTARY DNA SEQUENCES OF THE HYPXANTHINE GUANINE PHOSPHO
RIBOSYL TRANSFERASE GENE FROM A MOUSE NEURO ELASTOMA CELL LINE FOUND TO
HAVE AMPLIFIED GENOMIC SEQUENCES

ERENFELD U, CHINULT A C, KONECKI D C, MELTON D W, CASKEY C T

HOWARD HUGHES MED. INST. LAB., BAYLOR COLL. MED., HOUSTON, TEX. 77030.

PROC NATL ACAD SCI U S A 79 (4), 1982. 1950-1954. CODEN: PNAS

Language: ENGLISH

Cloned complementary DNA sequences of the murine hypoxanthine/guanine phosphoribosyltransferase (HPRT; EC 2.4.2.2) gene were isolated by using a mouse neuroblastoma cell line containing increased levels of a variant HPRT protein. These sequences were used as probes to demonstrate that protein over-production in this cell line is a consequence of at least a 20-fold increase in HPRT mRNA levels resulting from approximately 50-fold amplification of HPRT genomic sequences. The largest cDNA insert so far characterized represents about 70% of the HPRT mRNA sequence. This cDNA possesses regions of homology with mRNA and DNA from Chinese hamster, baboon and human, thus facilitating detailed analysis of this locus in these 4 spp.

22/7/16 (Item 14 from 11/4/5)

0011011001 DISCO Number: 72051005

STATISTICAL ANALYSIS OF MUTANT AND REVERTANT FORMS OF CHINESE HAMSTER HYPX
ANTHINE GUANINE PHOSPHO RIBOSYL TRANSFERASE EC-2.4.2.2

YOUNG D B, FENWICK D C JR, CASKEY C T

HOWARD HUGHES MED. INST., HOUSTON, TEX. 77030.

J BIOL CHEM 257 (4), 1982. 2270-2284. CODEN: JBCHA

Language: ENGLISH

Analysis of 25,000 cells of Chinese hamster cells that were selected for resistance to 6-thioguanine following treatment of wild type cells with 6-thioguanine or 6-thioguanine, respectively. The cell lines were tested for their ability to synthesize hypoxanthine-guanine phosphoribosyltransferase (EC 2.4.2.2) that is either inactive, in the case of RJK9, or has altered binding properties in the case of RJK3. The altered binding properties of RJK3 and RJK9 were associated with increased mobility of

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There are many "big reasons" for choosing to develop the human as the "highland" experimental system in genetics: an obvious social context that allows interest, wide medical observation of the population that permits identification of an abundance of genetic defects, and our ability to pinpoint in the human subtle or complex variations that may not be detectable in other species. Various lines of genetic inquiry that are based or inspired by other systems—cytogenetic analysis, biochemical cloning, mapping of defective loci by linkage analysis in affected families, and in vitro techniques such as the creation of transgenic

organisms complemented and enrich each other. New phenomena that could not have been predicted from investigations in other organisms have been found in humans, such as the discovery of the "giant" Duchenne muscular dystrophy gene and the identification of successive cancer genes. Genetic research is yielding insights into human biology that are raising new possibilities for therapy and prevention of disease, as well as challenges to society in the form of ethical decisions about the appropriate application of genetic information. (60 Refs.)

23/7/19 (Item 2 from file: 155)

01229407 87210407

The molecular basis of the sparse fur mouse mutation.

Miller G, Sills RA; Scherer SE; Caskey CT

Science Jul 24 1987, 237 (4818) p415-7, ISSN 0036-8075

Journal Code: M7

Contract/Grant No.: HD21452

Language: ENGLISH

The ornithine transcarbamylase-deficient sparse fur mouse is an excellent model to study the most common human urea cycle disorder. The mutation has been well characterized by both biochemical and enzymological methods, but its exact nature has not been revealed. A single base substitution in the complementary DNA for ornithine transcarbamylase from the sparse fur mouse has been identified by means of a combination of two recently described techniques for rapid mutational analysis. This strategy is simpler than conventional complementary DNA library construction, screening, and sequencing, which has often been used to find a new mutation. The ornithine transcarbamylase gene in the sparse fur mouse contains a C to A transversion that alters a histidine residue to an asparagine residue at amino acid 117.

23/7/20 (Item 3 from file: 155)

03090322 87064322

Fine structure of the human hypoxanthine phosphoribosyltransferase gene.

Patel PI; Frazer PE; Caskey CT; Chinault AC

Mol Cell Biol Feb 1988, 8 (2) p392-400, ISSN 0270-7306

Journal Code: NGV

Contract/Grant No.: AMS1428

Language: ENGLISH

The human hypoxanthine phosphoribosyltransferase (HPRT) gene has been characterized by molecular cloning, mapping, and DNA sequencing techniques. The entire gene, which is about 44 kilobases in length, is composed of nine exon elements. The positions of the introns within the coding sequence are identical to those of the previously-characterized mouse HPRT gene, although there are significant differences between intron sizes for the two genes. HPRT minigenes have been used in a transient expression assay involving microinjection into HPRT- cells to demonstrate functional promoter activity within a 231-base-pair region upstream from the ATG codon. The promoter of this gene resembles those of other recently characterized "housekeeping" genes in that it lacks CAAT- and TATA-like sequences, but contains several copies of the sequence GGGCCC. Both RNase protection and primer extension analysis indicate that human HPRT mRNA is heterogeneous at the 5' terminus, with transcription initiation occurring at sites located roughly 1 to 10% to congruent to 169 base pairs upstream from the ATG codon. Comparison of the mouse and human HPRT 5'-flanking sequences indicates that there are only limited stretches of conserved sequence, although there are other shared features, such as an extremely high density of potential acetylation sites, that may have functional significance.

23/7/21 (Item 4 from file: 155)

05713347 01014347

Expression of human HPRT in the central nervous system of transgenic mice.

Stout JT; Chan HY; Frazer PE; Caskey CT; Miller RL

Nature Sep 10-25 1988, 337 (6234) p250-2, ISSN 0028-0836

Journal Code: M7

Language: ENGLISH

Severe deficiency of hypoxanthine phosphoribosyltransferase (HPRT) in man results in the Lesch-Nyhan syndrome, an X-linked neurological disorder characterized by mental retardation, choreoathetosis and a compulsive tendency towards self-mutilation. Although the HPRT gene is normally constitutively expressed in all tissues at low levels, expression is elevated approximately fourfold in several regions of the central nervous system, particularly in the basal ganglia. The relationships between HPRT deficiency, tissue-specific alterations of nucleotide metabolism and the neuropathology of the Lesch-Nyhan syndrome remain unclear. Here we have constructed recombinant molecules containing human HPRT (hHPRT) complementary DNA, the mouse metallothionein-I (MT-I) promoter and the 3' untranslated portion of the human growth hormone (hGH) gene into mouse plasmids to produce transgenic animals that express hHPRT on induction by cadmium. The hHPRT cDNA in these experiments contained 98 base pairs (bp) of 5'-untranslated and 190 bp of 3'-untranslated sequences, and the full-length coding sequence. We studied the *in vivo* expression of this MT-hHPRT fusion gene and observed preferential hHPRT expression in tissues of the central nervous system (CNS). This study suggests that sequences within the HPRT transcript (cDNA) influence CNS expression via increased synthesis or stability of messenger RNA.

22/7/22 (Item 5 from file: 155)

0057107 83090437

Hypoxanthine-guanine phosphoribosyltransferase genes of mouse and Chinese hamster: construction and sequence analysis of cDNA recombinants.

Kinsacki DS; Brannard J; Fuscoe JD; Caskey CT; Chinault AC

Nucleic Acids Res Nov 11 1982; 10 (21) p6763-75; ISSN 0301-5410

Journal Code: OSL

Contract/Grant No.: GM07526

Language: ENGLISH

Recombinant plasmids containing DNA inserts complementary to mRNA coding for hypoxanthine-guanine phosphoribosyltransferase (HPRT) from mouse and Chinese hamster cell lines have been isolated from cDNA libraries and characterized by DNA sequence analysis. A total of 1292 nucleotides of the mouse cDNA sequence and 1301 nucleotides of the Chinese hamster cDNA sequence has been determined. Each of these sequences includes an open reading frame of 354 nucleotides (218 amino acids) corresponding to the HPRT protein coding region. The deduced amino acid sequences for the mouse and Chinese hamster enzymes are presented and compared to that of human HPRT. At least 95% of the amino acids are conserved in the three species. In addition, we present evidence that two species of HPRT mRNA, which differ in the site of polyadenylation that is utilized during processing of the RNA transcripts, exist in Chinese hamster cells.

22/7/22 (Item 6 from file: 155)

00202436 78022433

Toward and reverse mutations affecting the kinetics and apparent molecular weight of mammalian HGPRT.

Fennick RC Jr; Sawyer TH; Kruh DD; Astrin KH; Caskey CT

Cell Oct 1977; 12 (2) p283-91; ISSN 0092-8674 Journal Code: CQ4

Language: ENGLISH

Chinese hamster cells selected for resistance to 8-azaguanine following mutagenesis have hypoxanthine-guanine phosphoribosyltransferase (HGPRT; E.C. 2.4.2.8) with characteristics compatible with different mutations in the structural gene for that enzyme. Using immunoprecipitation and SDS-polyacrylamide electrophoresis, mutants producing antigenically active forms of the enzyme can be analyzed for changes in the molecular weight of HGPRT. Enzyme subunits from mutants RJK3 and RJK39 are reduced in molecular weight by an estimated 4 and 2%, respectively. HGPRT activity is not detectable in RJK37. The enzyme from RJK3 is active but has altered substrate binding properties. Enzymes from two other mutants with altered kinetic properties, RJK41 and RJK47, have normal molecular weights. The genetic alterations of RJK41 and 47 are probably missense mutations, while RJK3 and 39 are likely either deletion or mutations causing premature

1987/11/11 11:11:11 Genetic cell hybridization between RSK39 and a revertant of that strain with VSPPT of normal molecular weight revealed that the revertant probably arose by intragenic mutation rather than extragenic recombination. 21/12/7/11/01

32/7/11 (Item 1 from file: 5)
0016191010 BIOSIS Number: 87093317

EVIDENCE AGAINST LOCATION OF THE GENE FOR FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY ON THE DISTAL LONG ARM OF CHROMOSOME 14

LUNT P W; MAGEES J G; UPADHAYA M; SARTORAZI M; HARPER P S
DEP. MED. GENETICS, ST. MARY'S HOSP., WHITEWORTH PARK, MANCHESTER M13 0JH, UK.

J NEUROL SCI 88 (1-3), 1989. 287-292. CODEN: JNSCA
Language: ENGLISH

A panel of 399 individuals from 24 kindreds with facioscapulohumeral muscular dystrophy (FSHD) has been established for genetic linkage studies. A previous suggestion of linkage on the distal long arm of chromosome 14 to the locus (IGHG) for the constant region of the heavy chain of IgG immunoglobulin was tested from serum Gm allotypes and from DNA analysis using an IGHG DNA probe. After applying an age-dependent weighting for presently unaffected but at risk individuals close linkage between the IGHG and FSHD loci was excluded.

32/7/12 (Item 2 from file: 5)
0018081001 BIOSIS Number: 85012754

AN IMPROVED METHOD FOR PRENATAL DIAGNOSIS OF GENETIC DISEASES BY ANALYSIS OF AMPLIFIED DNA SEQUENCES APPLICATION TO HEMOPHILIA A

KODAN C G; QUINCY M; GITSCHER J
HOWARD HUGHES MED. INST., BOX 0724, UNIV. CALIFORNIA, THIRD PARNASSUS AVE., SAN FRANCISCO, CALIF. 94143.

N ENGL J MED 317 (1A), 1987. 905-906. CODEN: NEJMA
Language: ENGLISH

We report the development of a rapid nonradioactive technique for the genetic prediction of human disease and its diagnostic application to hemophilia A. This method is based on enzymatic application of short segments of human genes associated with inherited disorders. A novel feature of the procedure is the use of a heat-stable DNA polymerase, which allow the repeated rounds of DNA polymerase, which allows the repeated sequence of DNA synthesis to proceed at 36.degree. C. The high sequence specificity of the amplification reaction of this elevated temperature permits restriction-site polymorphisms, contained in the amplified samples, to be analyzed by visual inspection of their digestion products on polyacrylamide gels. By means of this method, we have performed carrier detection and prenatal diagnosis of hemophilia in two families with use of the factor VIII intragenic polymorphisms identified by the restriction enzymes BclI and KbaI. Predictions can be made directly from chorionic villi, without previous DNA extraction, and fetal sex can be determined by amplification of sequences specific for the Y chromosome. Specific amplification of genomic sequences with heat-stable DNA polymerase is applicable to the diagnosis of a wide variety of inherited disorders. These include diseases diagnosed by restriction-site variation, such as Duchenne's muscular dystrophy and sickle cell anemia, those due to a collection of known mutations, such as beta-thalassemia, and those due to gene deletion, such as alpha-thalassemia.

32/7/13 (Item 3 from file: 5)
0014553306 BIOSIS Number: 82032398

EXPRESSION OF THE MOUSE HYPOXANTHINE PHOSPHORIBOSYLTRANSFERASE GENE DELETIONAL ANALYSIS OF THE PROMOTER REGION OF AN X-CHROMOSOME LINKED HOUSEKEEPING GENE

NELSON D H; MCEWAN C; MCKIE A B; REID A Y
DEP. MOL. BIOL., UNIV. EDINBURGH, MAYFIELD RD., EDINBURGH EH9 3JR, UK.
CELL 44 (2), 1974. 319-323. CODEN: CELL

Language: ENGLISH
The mouse hypoxanthine phosphoribosyltransferase gene, like several other

housekeeping genes, but many of the features associated with promoters of RNA polymerase II-transcribed genes. MFR transcripts have multiple initiation sites and an MPT-tinogen was used to show that only 49 bases of 5' flanking sequence was necessary for normal expression in cultured cells. The essential region, which occurs within a complex series of direct repeats, is homologous to sequences upstream of other housekeeping genes. When this region was deleted, cryptic upstream initiation sites were revealed. Similar cleavage patterns of initiation were seen with all tinogenes in *Xenopus* oocytes. We speculate that this region of the MPT promoter is involved in a different interaction with the transcriptional machinery, as that occurring at more conventional promoters.

82/7/4 (Item 4 from file 5)

001670410 BIOSIS Number: 82013467

CLONING AND SCREENING WITH NANOGRAM AMOUNTS OF IMMUNOPURIFIED MESSENGER RNA COMPLEMENTARY DNA CLONING AND CHROMOSOMAL MAPPING OF CYSTATHIONINE BETA SYNTHASE AND THE BETA SUBUNIT OF PROPIONYL COENZYME A CARBOXYLASE

KRAUS J P; WILLIAMSON C L; FIRCAIRA F A; VAN-FENG T L; MUNKE N; FRANCKE U ; ROSENBERG L E

YALE UNIV. SCH. MED., DEPT. HUMAN GENETICS, 333 CEDAR ST., P.O. BOX 3333, NEW HAVEN, CONN. 06510.

PROC NATL ACAD SCI U S A 83 (7). 1986. 2047-2051. CODEN: PNASA

Language: ENGLISH

We have developed conditions for efficient cDNA cloning of nanogram amounts of purified mRNAs coding for cystathionine .beta.-synthase II-synthase hydro-lyase (adding homocysteine), EC 4.2.1.221 and for the cytosolic precursors of mitochondrial ornithine transcarbamylase (carbamoylphosphate:ornithine carbamoyltransferase, EC 2.1.3.2) and the .beta.-subunit of propionyl-CoA carboxylase (propanoyl-CoA: carbon-dioxide ligase (ADP-forming), EC 6.4.1.31). The three mRNAs, prepared by sequential immunoselection from the same batch of rat liver polysomes, were pooled (20 ng each), and cDNA was synthesized by using avian reverse transcriptase. The second DNA strand was prepared by "nick-translation repair" of the cDNA template. cDNA hybrid with RNase H, polymerase I, and DNA ligase from *Escherichia coli*. The double-stranded (ds) DNA was tailed with deoxytyridine residues, annealed with Pst I-cut/dG-tailed pBR322, and used to transform *E. coli*. The library generated by this three-step procedure contained 5000 independent colonies. A 550-base-pair (bp) cDNA clone of the .beta.-subunit of propionyl-CoA carboxylase was detected by hybrid-selected translation; it was then used to screen the library for longer cDNAs. Two hybridizing cDNAs, 1200 and 1000 bp long with a 200-bp overlap, representing together a full-length copy of the coding region and 446 bp of 3' untranslated sequence, were recovered. Each plasmid mapped to the region q18.3 .fwdarw. q22 of human chromosome 3. Cystathionine .beta.-synthase clones were obtained by screening the library with a single-stranded 132P-cDNA prepared directly from the highly purified synthase mRNA by reverse transcriptase. The longest hybridizing cDNA of 1700 bp was used in hybrid-selected translation and detected a polypeptide of 63 kDa, identical in size to rat liver synthase. In situ hybridization of this cDNA to q22 of human chromosome 21 confirmed two previous tentative assignments of the synthase locus to this chromosome.

82/7/5 (Item 5 from file 5)

001616455 BIOSIS Number: 83036220

THE HUMAN DNA POLYMERASE ALPHA GENE IS LOCATED ON THE SHORT ARM OF THE X CHROMOSOME

HANG T S-F; PEARSON D E; SUOMALAINEN H A; MOHANDAS T; SHAPIRO L J; SCHRÖDER J; KORN J

STANFORD MED. SCH., STANFORD, CALIF.

EIGHTH INTERNATIONAL WORKSHOP ON HUMAN GENE MAPPING, HELSINKI, FINLAND, AUG. 4-12, 1985. CYTOGENET CELL GENET 40 (1-4). 1985. 773. CODEN: CGCGB

Language: ENGLISH

81/7/3 (Item 3 from file 5)

001616372 BIOSIS Number: 82013471

LINKAGE STUDIES IN AUTOSOMAL DOMINANT FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

PADEIRO C; EMKSON A H; MOUKERS W G; BERNINI L; VAN LOGHEM E; MEERA KHAN P; NIJENHUIS L E; FRANK J C; SCHREUDER G M T

DEP. OF NEUROLOGY, UMCM HOSPITAL LEYDEN, RIJNSBURGERWEG 10, 2333 AA LEYDEN, THE NETHERLANDS.

J NEUROL SCI 115 (2). 1994. 241-249. CODEN: JNSCA

Language: ENGLISH

Linkage studies were undertaken in 120 individuals from 10 kindreds with autosomal dominant facioscapulohumeral muscular dystrophy using 35 different marker genes. No linkage was found. The highest lod score was 1.438 for the IgH chain gene cluster (IGH) at a recombination fraction of 0.2. IgH is located on the long arm of chromosome 14. Based on scores of other marker genes and on a recombination map of chromosome 14, the probability that the gene for facioscapulohumeral muscular dystrophy is located on chromosome 14 is estimated to be approx. 6%.

02/7/77 (Item 7 from file: 5)

001151070 BIOSIS Number: 71024270

BRANCHED CHAIN AMINO TRANSFERASE DEFICIENCY IN CHINESE HAMSTER CELLS COMPLEMENTED BY 2 INDEPENDENT GENES ON HUMAN CHROMOSOMES 12 AND 19

MAYLOP C L; SHONG T B

BIOCHEMICAL GENETICS SECTION, ROSWELL PARK MEMORIAL INSTITUTE, NEW YORK STATE DEPARTMENT OF HEALTH, BUFFALO, NEW YORK 14263.

SOMATIC CELL GENET 6 (5). 1990. 441-452. CODEN: SCGTD

Language: ENGLISH

Branched-chain aminotransferase (BCT) catalyzes the reversible transamination of the branched-chain .alpha.-keto acids to the branched-chain L-amino acids. Since branched-chain L-amino acids (L-isoleucine, L-leucine and L-valine) are essential for cell growth, cells which lack BCT were unable to proliferate in media containing .alpha.-keto acids in place of the corresponding L-amino acids. CHW-1102, a Chinese hamster cell line, lacks BCT and does not grow in .alpha.-keto acid media. Somatic cell hybrids were made by the fusion of CHW-1102 (Hprt-hypoxanthine-guanine phosphoribosyltransferase-deficient) with several human cell lines and isolated on HAT [hypoxanthine-aminopterin-thymidinal] medium. Growth assays of hybrid clones on .alpha.-keto acid selection media independent of the HAT selection medium indicated 2 cell hybrid phenotypes: either the hybrid clone, like the parental CHW-1102, could not utilize .alpha.-keto acid media or the hybrid could proliferate on all 3 .alpha.-keto acid media. The ability of hybrid cells to proliferate on .alpha.-keto acid media correlated with the presence of either of 2 human genes which independently complemented the Chinese hamster deficiency. Two human genes, BCT1 assigned to chromosome 12 and BCT2 assigned to chromosome 19, coded for the expression of 2 molecular forms of BCT.

02/7/78 (Item 8 from file: 5)

0010106252 BIOSIS Number: 69623248

CHROMOSOMAL LOCATION OF THE GENES FOR HUMAN IMMUNOGLOBULIN HEAVY CHAINS

CRUCE C M; SHANDER M; MARTINIS J; CIOUREL L; D'ANCONA G G; DOLBY T W; KOTCHINSKI P

UNIVERS. INCT. NAT. BIOL., 36TH ST. AT SPRUCE, PHILADELPHIA, PA. 19104, USA.

PROC NATL ACAD SCI U S A 76 (7). 1979. 3416-3419. CODEN: PNASA

Language: ENGLISH

Somatic cell hybrids between 23x524g9 mouse myeloma cells deficient in hypoxanthine phosphoribosyltransferase (EC 2.4.2.8) and either human peripheral lymphocytes or human lymphoblastoid or myeloma cells were studied for the production of human immunoglobulin [Ig] chains and for the expression of enzyme markers assigned to each of the different human chromosomes. Human chromosome 14 was the only human chromosome present in all independent hybrids producing .mu., .gamma. and .alpha. human H chains. In 2 of the independent hybrids that produced .mu. and .gamma. human H chains, chromosome 14 was the only human chromosome present in the hybrid cells. Loss of human chromosomes 14 from these hybrids resulted in the concomitant loss of their

ability to produce human Ig H chains. The genes for human Ig H chains are approximately located on human chromosome 14 in reproducing human cells.

32/7/10 (Item 1 from file: 155)

01000002 00100002

On the long arm of the gene for facioscapulohumeral muscular dystrophy on the distal long arm of chromosome 14.

L. J. R. Jones, T. Upadhyaya, M. Sanfey, M. Harper, P. S.

Department of Medical Genetics, University of Wales College of Medicine, Cardiff, U.K.

Muscle Nerve (UNITED STATES) Dec 1995, 18 (11-12) p287-92, ISSN 0022-510X

Journal Code: J21

Language: ENGLISH

A panel of 399 individuals from 24 kindreds with facioscapulohumeral muscular dystrophy (FSHD) has been established for genetic linkage studies. A previous suggestion of linkage on the distal long arm of chromosome 14 to the locus (IGHG) for the constant region of the heavy chain of IgG immunoglobulin was tested from serum Gm allotypes and from DNA analysis using an IGHG DNA probe. After applying an age-dependent weighting for presently unaffected but at risk individuals close linkage between the IGHG and FSHD loci was excluded.

32/7/10 (Item 2 from file: 155)

06712566 00014566

Linkage studies in facioscapulohumeral muscular dystrophy.

P. J. B. van den Berg, E. C. Vulliamis, W. S. De Lange, G. Wintzen, A. R.

Department of Neurology, State University of Leiden, the Netherlands.

Muscle Nerve (UNITED STATES) Aug 1998, 11 (8) p833-5, ISSN 0148-639X

Journal Code: J21

Language: ENGLISH

Possible linkage between the locus for autosomal dominant facioscapulo-humeral muscular dystrophy and the locus for the constant region of the heavy chains of the IgG immunoglobulins (Gm) was tested in 1 kindred (23 affected and 18 unaffected sibs) using the polymorphic DNA probe D14S1, which is known to be closely linked with Gm. No linkage between the loci for the disease and the probe was found, and the lod scores suggested that the locus for facioscapulohumeral muscular dystrophy is not situated on the distal part of the long arm of chromosome 14.

32/7/11 (Item 3 from file: 155)

01000002 00014002

An improved method for prenatal diagnosis of genetic diseases by analysis of amplified DNA sequences. Application to hemophilia A.

Kogan, S. D.; Boherty, M.; Gitschler, J.

Howard Hughes Medical Institute, University of California, San Francisco, CA 94143.

N Engl J Med Oct 15 1997, 337 (16) p995-90, ISSN 0028-4793

Journal Code: J21

Language: ENGLISH

We report the development of a rapid nonradioactive technique for the genetic prediction of human disease and its diagnostic application to hemophilia A. This method is based on enzymatic amplification of short segments of human genes associated with inherited disorders. A novel feature of the procedure is the use of a heat-stable DNA polymerase, which allows the repeated rounds of DNA synthesis to proceed at 63 degrees C. The high sequence specificity of the amplification reaction at this elevated temperature permits restriction-site polymorphisms, contained in the amplified samples, to be analyzed by visual inspection of their digestion products on polyacrylamide gels. By means of this method, we have performed carrier detection and prenatal diagnosis of hemophilia in two families with use of the factor VIII intragenic polymorphisms identified by the restriction enzymes BclI and XbaI. Predictions can be made directly from DNA in Vili, without previous DNA extraction, and fetal sex can be identified by amplification of sequences specific for the Y chromosome. Rapid amplification of genomic sequences with heat-stable DNA polymerase is a valuable tool for the diagnosis of a wide variety of inherited disorders.

These include diseases diagnosed by restriction-site variation, such as Duchenne's muscular dystrophy and sickle cell anemia, those due to a deletion of entire chromosomes, such as beta-thalassemia, and those due to gene deletion, such as alpha-thalassemia.

32/7/13 (Item 5 from file: 155)

05923017 06024017

The localization of the tRNA102 gene near the 3' OH terminus of a fast myosin heavy chain gene. A comparison between normal and dystrophic chickens.

Lezza BJ; Heywood SM


J Biol Chem Jun 5 1986, 261 (16) p7455-60, ISSN 0021-9258

Journal Code: HIV

Contract/Grant No.: HD03316-17

Language: ENGLISH

Two genomic fragments were isolated from a normal and a dystrophic library containing the 3'OH terminus of the fast isoform of myosin heavy chain gene. Restriction map analysis confirmed that the genes were similar. The sequences coding for tyrosin were defined and shown to be the same in each genomic fragment. However, using a cDNA clone for tRNA102 and two specific oligomers for tRNA102 sequences, we determined that only the genomic fragment from normal chick contained homologous sequences to tRNA102. Dystrophic chick DNA did not contain these regions of homology. In addition, the normal genomic fragment transcribes tRNA102 in vitro via RNA polymerase III while the corresponding fragment of DNA from dystrophic chick was inactive. These results suggest that there are detectable differences between the normal and dystrophic genomes in this regard.



32/7/13 (Item 5 from file: 155)

05974544 06177544

Cloning and screening with nanogram amounts of immunopurified mRNAs: cDNA cloning and chromosomal mapping of cystathionine beta-synthase and the beta subunit of propionyl-CoA carboxylase.

Kraus JP; Williamson CL; Fingaira FA; Yang-Feng TL; Munke N; Francke U; Rosenberg LE


Proc Natl Acad Sci U S A Apr 1986, 83 (7) p2047-51, ISSN 0027-3424

Journal Code: PVS

Contract/Grant No.: AM 09527; GM 26105; GM 07439

Language: ENGLISH

We have developed conditions for efficient cDNA cloning of nanogram amounts of purified mRNAs coding for cystathionine beta-synthase (L-serine hydro-lyase (adding homocysteine), EC 4.2.1.22) and for the cytosolic precursors of mitochondrial ornithine transcarbamylase (carbamoylphosphate: L-ornithine carbamoyltransferase, EC 2.1.3.3) and the beta subunit of propionyl-CoA carboxylase (propanoyl-CoA: carbon-dioxide ligase (ADP-forming), EC 6.4.1.3). The three mRNAs, prepared by sequential immunoselection from the same batch of rat liver polysomes, were pooled (20 ng each), and cDNA was synthesized by using avian reverse transcriptase. The second DNA strand was prepared by "nick-translation repair" of the cDNA. mRNA hybrid with RNase H, polymerase I, and DNA ligase from Escherichia coli. The double-stranded (ds) DNA was tailed with deoxycytidine residues, annealed with Pst I-cut/UG-tailed pBR322, and used to transform E. coli. The library generated by this three-step procedure contained 5000 independent colonies. A 350-base-pair (bp) cDNA clone of the beta subunit of propionyl-CoA carboxylase was detected by hybrid-selected translation; it was then used to screen the library for longer cDNAs. Two hybridizing cDNAs, 1300 and 1000 bp long with a 200-bp overlap, representing together a full-length copy of the coding region and 446 bp of 3' untranslated sequence, were recovered. Each plasmid mapped to the region q13.3---q22 of human chromosome 3. Cystathionine beta-synthase clones were obtained by screening the library with a single-stranded [32P]cRNA prepared directly from the highly purified synthase mRNA by reverse transcriptase. The longest hybridizing cDNA of 1700 bp was used in hybrid-selected translation and detected a polypeptide of 63 kDa, identical in size to rat liver synthase. In situ hybridization of this cDNA to q22 of human chromosome 21 confirmed the previous tentative assignments of the synthase locus to this



chromosome.

02/7/14 (Item 6 from file: 155)

05305208 0101008

Expression of the mouse HPRT gene: deletion analysis of the promoter region of an X-chromosome linked housekeeping gene.

Melton DM, McEuen Q, M. M. AP, G. L. AM

Cell Jan 31 1986, 44 (2) p319-22, ISSN 0092-8674 Journal Code: CCM

Language: ENGLISH

The mouse hypoxanthine phosphoribosyltransferase gene, like several other housekeeping genes, lacks many of the features associated with promoters of RNA polymerase II-transcribed genes. HPRT transcripts have multiple initiation sites and an HPRT oligonucleotide was used to show that only 49 bases of 5' flanking sequence was necessary for normal expression in cultured cells. The essential region, which occurs within a complex series of direct repeats, is homologous to sequences upstream of other housekeeping genes. When this sequence was deleted, cryptic upstream initiation sites were revealed. Similar aberrant patterns of initiation were seen with all minigenes assayed in Xenopus oocytes. We speculate that this region of the HPRT promoter is involved in a different interaction with the transcriptional machinery to that occurring at more conventional promoters.

sup X

02/7/15 (Item 7 from file: 155)

05790476 01091474

Human DNA polymerase alpha. Cloning and localization of the gene on the X chromosome.

Yanagida E, Tanabe M, Miyazawa M, Morikawa Y, Hori T, Yamada M

Mol Biol Cell Oct 1984, 2 (5) p233-35, ISSN 0735-1013 Journal Code: MOL

Language: ENGLISH

The chromosomal location of human DNA polymerase alpha gene was determined by studies on somatic cell hybrids between a temperature-sensitive mutant cell line of mouse F10A cells and normal human lymphocytes or a line of human diploid fibroblasts derived from a patient with the fragile X syndrome. A temperature-sensitive mutant, FT20-M6, a 8-thioguanine-resistant derivative of tsFT20, has heat-labile DNA polymerase alpha. Interspecific cell hybrids between FT20-M6 and human cells grew at the non-permissive temperature, indicating that some human chromosomes can compensate for the temperature-sensitive defect of tsFT20 in mouse/human cell hybrids. Three of these hybrid clones were examined further, and were shown to contain heat-stable DNA polymerase alpha that was neutralized with human DNA polymerase alpha-specific monoclonal antibody. Subcloning and segregation tests of these hybrid clones showed a positive correlation between the expression of human DNA polymerase alpha and the presence of the human X chromosome. Two subclones, however, did not conform to this relationship: they grew at the nonpermissive temperature but not in hypoxanthine/azidothymidine/thymidine medium. Detailed examination of the human chromosomes in these subclones revealed that these clones had only one human chromosome, an X chromosome with a terminal deletion of the long arm including the locus of the gene for hypoxanthine phosphoribosyltransferase (EC 2.4.2.6). From these data, the functional DNA polymerase alpha gene was located on the human X chromosome.

X

02/7/16 (Item 8 from file: 155)

05782194 01033194

The mom gene of bacteriophage mu: a unique regulatory scheme to control a lethal function.

Kahmann R, Sailer A, Wolzky FR, Pfaff E

Gene 1985, 89 (1) p61-70, ISSN 0378-1119 Journal Code: FOP

Language: ENGLISH

The mom gene of bacteriophage mu encodes a DNA modification function which converts adenine to acetylated adenine in a sequence-specific manner. The mom gene itself is subject to a complex regulation: gene expression requires methylation by the Escherichia coli Dam methylase of specific sites upstream of the mom promoter and transactivation of the promoter by a Mu gene product. The requirement for transactivation can be overcome when

X

measurements of the rate of fixation of mutations that do not change the amino acid sequence. The minimum estimate for this rate is greater than the highest previously estimated rates of fixation of neutral mutations (calculated for fibrinopeptide A). A new technique, deoxysubstitution sequencing, which should speed determination of the complete mRNA sequences, is described.

2display sets

Set	Items	Description
31	580	AU-CASKEY, C? OR AU-CASKEY C?
32	927	AU-CHAMBERLAIN, J? OR AU-CHAMBERLAIN J?
33	666	AU-SIBBS, R? OR AU-SIBBS R?
34	19	AU-RANIER, J? OR AU-RANIER J?
35	13	S1 AND S2 AND S3 AND S4
36	9	S5 NOT PY-1989
37	1990	S1 OR S2 OR S3 OR S4
38	1322	S7 NOT PY-1989
39	1313	S8 NOT S6
310	134	S9 AND (PRIMER? OR POLYMERASE? OR CHAIN OR COMPLEMENT?)
311	190316	CHROMOSOME?
312	0	S S10 AND S11
313	10	S10 AND S11
314	1	S12 AND DELETION?
315	12	S13 NOT S14
316	1127	ORNITHINE(2U)TRANSCARBAMYLASE
317	3786	HYPOXANTHINE(2U)PHOSPHORIBOSYLTRANSFERASE
318	747	STEPOID(2H)SULFATASE
319	59050	MUCOPOLY(2H)DYSTROPHY OR MS
320	64962	S16 OR S17 OR S18 OR S19
321	60026	S20 NOT PY-1989
322	121	S10 NOT (S14 OR S15)
323	22	S21 AND S22
324	373709	PRIMER? OR POLYMERASE? OR CHAIN OR COMPLEMENT?
325	3	X-LINK?
326	3	S25 OR X LINK?
327	0	X-LINK?
328	4	X-LINK?
329	1706	X-CHROMOSOME?
330	59064	S21 NOT (S6 OR S14 OR S15 OR S10 OR S23)
331	5	S20 AND S24 AND (S26 OR S28 OR S29)
332	36	(S20 AND S24 AND CHROMOSOME?) OR S31

mom is transcribed from foreign promoters. When cloned into various sites in pUC8, the mom gene is always found in an orientation where transcription of the mom gene is excluded. The productive orientation is 1211' to 1211'. This effect is mediated by the concerted action of the mom gene, pUC8 and the product of gene com (control of mom, previously termed CCF-1) whose coding region overlaps the 5'-coding region of the mom gene. When mom is expressed from its own promoter, internal deletions in com completely abolish expression of the mom gene. Fragments containing the 5' end of com can be cloned downstream of constitutive plasmid promoters. The com gene product itself is not lethal to the cell. The region encoding com has been cloned in pl expression vectors. The mom gene product, a peptide of 27 kDa, has been visualized on gels. Efficient expression of the com gene requires gene com. A fusion between MS-2 polymerase and com has been generated. The fusion product is made in large amounts, whereas the mom gene product is not overproduced although the gene is present on the same transcriptional unit. (ABSTRACT TRUNCATED AT 250 WORDS)

02/7/17 (Item 9 from file: 155)

05154711 85270506

Assignment of the gene for human DNA polymerase alpha to the X chromosome.

Hang TS; Pearson DE; Suomalainen HA; Mohandas T; Shapiro LJ; Schroder J; Kohn D

Proc Natl Acad Sci U S A Aug 1985, 82 (16) p5270-4, ISSN 0027-8424

Journal Code: PVO

Contract/Grant No.: CA-14835

Language: ENGLISH

We have applied an assay based on a monoclonal antibody that discriminates the activity of human DNA polymerase alpha in rodent-human somatic cell hybrid clones to identify a single genetic locus that is both necessary and sufficient for the expression of DNA polymerase alpha. We have mapped this locus to the short arm of the human X chromosome, near the junction of bands Xp21.3 and Xp22.1, and demonstrated that it is not expressed from an inactive X chromosome.

02/7/18 (Item 10 from file: 155)

0509507 85155507

Sequence of the promoter region of the gene for human X-linked 3-phosphoglycerate kinase

Singer-Saiz J; Keith EH; Tani K; Simmer RL; Shively L; Lindsay S; Yoshida A; Riggs AD

Gene Dec 1984, 82 (3) p109-17, ISSN 0378-1119 Journal Code: FOP

Language: ENGLISH

We have determined the sequence of an 812-bp BamHI-EcoRI restriction fragment containing the 5' region of the human gene for PGK (3-phosphoglycerate kinase or ATP:3-phospho-D-glycerate 1-phosphotransferase; EC 2.7.2.3). The fragment contains 450 bp 5' to three start points for transcription (located by primer extension and S1 nuclease mapping), a leader sequence 95-94 bp long, the first exon of gene (65 bp), and part of the first intron. The promoter region is extremely G + C-rich, lacks a TATA box, and has an 8-bp direct repeat. A comparison of the promoter region for PGK with other promoters on the X-chromosome reveals homology with the promoter for HPRT, but not with the operator for factor IX.

02/7/19 (Item 11 from file: 155)

05016767 85032767

Linkage studies in autosomal dominant facioscapulohumeral muscular dystrophy.

Radberg G; Eriksson AN; Volkens MG; Bernini L; Van Loghem E; Maera Khan P; Nijm LM; Frank JC; Schneider OH

J Hum Genet Sep 1984, 65 (3) p261-8, ISSN 0022-510X Journal Code: JBO

Language: ENGLISH

Linkage studies were undertaken in 120 individuals from 10 kindreds with autosomal dominant facioscapulohumeral muscular dystrophy using 35

different marker genes. No linkage was found. The highest lod score was 1.428 for the immunoglobulin heavy chain gene cluster (IGH) at a recombination fraction of 0.2. IGH is located on the long arm of chromosome 14. Based on scores of other marker genes and on a recombination map of chromosome 14, the probability that the gene for facioscapulohumeral muscular dystrophy is located on chromosome 14 is estimated to be approximately 5%.

92/7/20 (Item 12 from file: 155)

05160517 04037664

Influence of inhibitors of poly(ADP-ribose) polymerase on DNA repair, chromosomal alterations, and mutations.

Natarajan AT; van Zeeland AA; Zwaanenburg TS

Int Symp Princess Takamatsu Cancer Res Fund 1993, 13 p227-42,

Journal Code: HWI

Language: ENGLISH

The influence of inhibitors of poly(ADP-ribose) polymerase such as 3-aminobenzamide (3AB) and benzamide (B) on the spontaneously occurring as well as mutagen induced chromosomal aberrations, sister chromatid exchanges (SCEs) and point mutations has been studied. In addition, we have measured the influence of 3AB on DNA repair following treatment with physical and chemical mutagens. Post treatment of X-irradiated mammalian cells with 3AB increases the frequencies of induced chromosomal aberrations by a factor of 2 to 3. Both acentric fragments and exchanges increase indicating that the presence of 3AB slows down the repair of DNA strand breaks (probably DNA double strand breaks), thus making breaks available for interaction with each other to give rise to exchanges. 3AB, when present in the medium containing bromodeoxyuridine (BrdUrd) during two cell cycles, increases the frequencies of SCEs in Chinese hamster ovary cells (CHO) in a concentration dependent manner leading to about a 10-fold increase at 10 mM concentration. Most 3AB induced SCEs occur during the second cell cycle, in which DNA containing bromouridine (BU) is used as template for replication. BU containing DNA appears to be prone to errors during replication. The extent of increase in the frequencies of SCEs by 3AB is correlated with the amount of BU incorporated in the DNA of the cells. The frequencies of spontaneously occurring DNA single strand breaks in cells grown in BrdUrd containing medium are higher than in the cells grown in normal medium and this increase depends on the amount of BU incorporated in the DNA of these cells. We have studied the extent of increase in the frequencies of SCEs due to 1 mM 3AB in several human cell lines, including those derived from patients suffering from genetic diseases such as ataxia telangiectasia (A-T), Fanconi's anemia (FA), and Huntington's chorea. None of these syndromes showed any increased response when compared to normal cells. 3AB, however, increased the frequencies of spontaneously occurring chromosomal aberrations in A-T and FA cells. 3AB does not influence the frequencies of SCEs induced by UV or mitomycin C (MMC) in CHO cells. However, it increases the frequencies of SCEs induced by ethyl methanesulfonate (EMS) and methyl methanesulfonate (MMS). Under the conditions in which 3AB increases the frequencies of spontaneously occurring as well as induced SCEs, it does not increase the frequencies of point mutations in hypoxanthine-guanine phosphoribosyltransferase (HGPRT) locus. 3AB does not influence the amount of repair replication following dimethylsulphate (DMS) treatment of human fibroblasts, or UV irradiated human lymphocytes. (ABSTRACT TRUNCATED AT 400 WORDS)

92/7/21 (Item 13 from file: 155)

02924041 06045041

Differential staining and segregation of parental chromosomes in mouse-rabbit hybridomas.

Modrano L; Phalento L; Buttin G

Cell Biol Int Rep Sep 1979, 3 (6) p503-14, Journal Code: CRC

Language: ENGLISH

Kirschot 33258 fluorescent staining can be coupled with G-banding to identify the chromosomal contribution of each parent in mouse-rabbit hybridomas. A fast and essentially complete segregation of rabbit chromosomes is obtained in these cells. The rabbit X chromosome is

preferentially maintained in media imposing HGPRT activity for cell growth. Mouse-rabbit hybridomas, some of which secrete rabbit immunoglobulin chains, should be a convenient material for the identification of chromosomes governing rabbit Ig chain synthesis.

82/7/22 (Item 14 from file: 155)

00920895 80034695

Chromosomal location of the genes for human immunoglobulin heavy chains.


Oreze OM; Shander M; Martinis J; Cicurel L; D'Arcena GG; Dolby TW; Kaprowski H

Proc Natl Acad Sci U S A Jul 1979, 76 (7) p3416-9, ISSN 0027-8424

Journal Code: FV3

Language: ENGLISH

We have studied somatic cell hybrids between P3x63Ag8 mouse myeloma cells deficient in hypoxanthine phosphoribosyltransferase (EC 2.4.2.6) and either human peripheral lymphocytes or human lymphoblastoid or myeloma cells for the production of human immunoglobulin chains and for the expression of enzyme markers assigned to each of the different human chromosomes. Human chromosome 14 was the only human chromosome present in all independent hybrids producing mu, gamma, and alpha human heavy chains. In two of the independent hybrids that produced human heavy chains, human chromosome 14 was the only human chromosome present in the hybrid cells. Loss of human chromosome 14 from these hybrids resulted in the concomitant loss of their ability to produce human immunoglobulin heavy chains. In view of these results, we conclude that the genes for human immunoglobulin heavy chains are located on human chromosome 14 in immunoglobulin-producing human cells.



82/7/22 (Item 15 from file: 155)

00217903 77119903

Structural and genetic studies on chicken 7S immunoglobulin allotypes.

II. Distribution of allotypes on the 7S immunoglobulin of homozygous and heterozygous chickens.


Wakeland EK; Benedict AA; Abplanalp HA

J Immunol Feb 1977, 118 (2) p401-4, ISSN 0022-1767 Journal Code:

IFB

Language: ENGLISH

We have previously reported that chicken 7S immunoglobulin (Ig) heavy (H) chain allotypes (CS-1 locus) segregate as phenogroups in F2 progeny. Specificity CS-1.1 formed a phenogroup with CS-1.4 in inbred chicken line UCD 2, and a second phenogroup with CS-1.3 in line UCD 3. To determine whether these phenogroups were formed by combinations of specificities on the same, or on separate subclasses of 7S Ig, their distribution on the 7S Ig molecules of birds homozygous for 7S Ig allotypes was analyzed by radioimmunoassay. Anti-CS-1.1 and anti-CS-1.3 alloantisera each bound more than 94% of line UCD 3 125I-7S Ig. Similar results were obtained with alloantisera to CS-1.1 and CS-1.4 WITH 125 I-7S Ig from line UCD 2. These results indicate that both phenogroups were formed by combinations of specificities present on the same H chain. Thus, each phenogroup described, probably is the product of a single structural gene which is responsible for more than 94% of the 7S Ig H chain constant regions. In F hybrids with the genotype CS-1.3, 1.3/CS-1.2, two populations of serum 7S Ig molecules were detected by direct and sequential binding analysis with specific alloantisera. One population of 7S Ig contained specificities CS-1.1 AND CS-1.3, but not CS-1.2; while the second population was exclusively the product of one parental allele. Consistent with a genetic regulatory mechanism involving allelic exclusion, no 7S Ig containing allotypes produced by both alleles was detected.



82/7/24 (Item 16 from file: 155)

00177132 77079132

Env-1, a restriction locus of a type C RNA virus in the feline cellular genome: identification, location, and phenotypic characterization in cat X mouse somatic cell hybrids.


O'Brien AD

Proc Natl Acad Sci U S A Dec 1976, 73 (12) p4618-22, ISSN 0027-8424

Journal Code: FV3

Languages: ENGLISH

Somatic cell hybrids were constructed between BALB/c-RAG mouse cells and feline lymphoma cells by the hypoxanthine-aminopterin-thymidine selection scheme. RAG cells spontaneously produce an endogenous B-tropic type C virus. Cat-mouse hybrids preferentially segregate feline chromosomes and retain murine chromosomes-demonstrable by karyotypic and isozyme analyses. Despite the presence of the complete mouse genome, including the viral genome, virus production was diminished to 1-5% of the levels observed in RAG parents based upon particle-associated RNA-dependent DNA polymerase (reverse transcriptase) activity in the culture fluid. Thirty-seven hybrids made on four different occasions had suppressed virus levels, and no hybrids expressed parental virus levels. Reverse selection experiments on 6-thioguanine demonstrated that a restriction gene, tentatively named *Bvr-1*, was linked to the feline structural genes for hypoxanthine phosphoribosyltransferase (IMP:pyrophosphate phosphoribosyltransferase; EC 2.4.4.3) and glucose-6-phosphate dehydrogenase (D-glucose-6-phosphate:NADP+ 1-oxidoreductase; EC 1.1.1.49) in cats, probably on the X-chromosome. The genetic mode of action of *Bvr-1* is trans dominant in restriction of murine leukemia virus. The restriction locus results in a block late in virus maturation but prior to release, since expression of antigens for viral structural proteins and mature budding particles is apparent on surfaces of restricted hybrid cells but not in high-speed pellets from culture fluid of restricted cells.



82/7/25 (Item 17 from file: 155)

02945495 76126495


Mouse MSV transformed cells resistant to 8-azaguanine.

Altaner C; Hladka M

Neoplasma 1975, 22 (6) p579-87, ISSN 0028-2435 Journal Code: NVO

Languages: ENGLISH

Mouse cells transformed by murine sarcoma virus were made resistant to 8-azaguanine. Resistant cells and cell clones isolated from them were deficient in hypoxanthine-guanine phosphoribosyl transferase (HGPRT) activity. They did not grow in HATG medium, did not incorporate labeled hypoxanthine, and had negligible HGPRT activity. The resistance was genetically stable. The resistant cells were hyperdiploid and contained telocentric chromosomes only. The resistant cells as well as the progenitor cells were slightly tumorigenic in mice, the plating efficiency in soft agar was very low. The parental cells and aza-G resistant cells produced C-type viral particles having RNA-dependent DNA polymerase activity. The resistance to aza-G did not influence the expression of murine sarcoma virus genome in cells. The resistant cells are suitable for preparation of cell hybrids.



82/7/26 (Item 18 from file: 155)

02911401 76092401

Investigation of the organization of mammalian chromosomes at the DNA sequence level.

Salser W; Bowen S; Browne D; el-Adli F; Fedoroff N; Fry K; Heindell H; Paddock G; Peon R; Wallace B; Whitcomb P

Eur J Mol Biol 1976, 35 (1) p23-35, ISSN 0014-9446 Journal Code: EUJ

Languages: ENGLISH

New developments in DNA sequencing techniques permit rapid progress in the determination of both repetitive and single-copy mammalian sequences. Three distinct families of highly repetitive satellite DNA's from the kangaroo rat *Dipodomys ordii* have been sequenced. With the M3 satellite it was possible to show that the basic repeat sequence and its variants were arranged in a nonrandom order suggesting a hierarchy of repeats. The M3-alpha satellite from *D. ordii* was shown to resemble the guinea pig alpha satellite, a long term evolutionary persistence inconsistent with previous models. Sequences from hemoglobin mRNA were determined using hemoglobin complementary DNA as template for transcription in vitro. Seven of the largest fragments have been assigned to untranslated regions of the mRNA whereas 15 others have been tentatively located within the structural genes. From correlations with sequences from corresponding regions in the human hemoglobin mRNA's we have been able to make the first direct

